COMMENTS

Claims 29-38, 41-48, and 62-67 are pending and under examination in the present case. Claims 29, 30, 32, 34, 36, 37, 38, 41, 43, 45, 48 and 66 are amended herein. Claims 31, 35, 44, 63-65, and 67, are canceled herein without prejudice or disclaimer. Claim 68 is newly added. Entry of the amendments and reconsideration of the application in view of the amendments herein are respectfully requested. Upon entry of the amendments, claims 29, 30, 32-34, 36-38, 41-43, 45-48, 62, 66, and 68 will be pending.

No new matter is added with the amendments to the specification and claims. Various paragraphs of the specification were amended to include full names to eliminate hypertext links. The Abstract was shortened. The amendment to claim 29, which recites that the coding region is contiguous, is supported, for example, by Figure 2, which provides a contiguous coding region encoding the polypeptide of SEQ ID NO:2. The amendment to claim 30, clarifying that the encoded polypeptide influences transcription is supported, for example, by page 6, second full paragraph. The amendment to claim 32, which recites that the polynucleotide encodes a polypeptide having the amino acid sequence of SEQ ID NO:9, is supported, for example, by claim 6 as filed. Newly added claim 68 is supported, for example, by claim 1 as filed. The remaining amendments to the claims delete or clarify claim language or correct typographical and/or obvious errors.

Objections to the Specification/Claims

The disclosure stands objected to because the abstract is allegedly too long. Applicants respectfully traverse the rejection. The Abstract is amended herein to be less than 150 words. Therefore, Applicants respectfully request that the objection be withdrawn.

The specification was objected to for the presence of hyperlinks. The hyperlinks have been removed in the amendments provided herein. Claim 29 was objected to for not including degree symbols. The pending claims do not refer to degrees. Therefore, the objection is moot. Finally, claim 35 was objected to for abbreviating "APECED." This abbreviation is not recited

in the pending claims as amended. Therefore, the objection is moot. Accordingly, Applicants respectfully request that the objections to the specification be withdrawn.

Claim Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 29-38, 41-43, 48, and 62-67 stand rejected under 35 U.S.C. § 112, first Paragraph as containing subject matter which was not described by the disclosure in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention. The Applicants respectfully traverse the rejection.

The Office Action acknowledges that the Applicants are in possession of the polynucleotide of SEQ ID NOS:1 and 6 and a method of producing a polypeptide of SEQ ID NOS:2 and 9. However, the Office Action alleges that the Applicants were not in possession, as of the filing date, of nucleotides that fall within the entire scope of the claims. The Office Action asserts that the claims encompass a large number of polynucleotide variants that are both structurally and functionally deviated from SEQ ID NO:1. However, the Office Action alleges that the specification provides insufficient teaching to support this breadth.

To expedite issuance of the present application and without prejudice or disclaimer, Applicants have canceled claims 31, 35, 63-65, and 67, thereby rendering moot, rejections related to these claims. Furthermore, to expedite issuance of the present application, the pending claims as amended, are directed to nucleic acid molecules that encode polypeptides having sequences that are disclosed in the application, contiguous fragments of SEQ ID NOS:1 and 6 that are at least 27 nucleotides in length, and particular variants of these nucleic acid molecules with specific insertions, deletions, or substitutions that are disclosed in the present specification.

More specifically, pending claims 29, 42, 43, and 48 relate to nucleic acid molecules, and methods using the same, that encode the polypeptide of SEQ ID NO:2. For example, claim 29 recites an isolated nucleic acid molecule that includes a contiguous coding region that encodes a polypeptide according to SEQ ID NO:2. Claim 48 recites a method of producing a polypeptide by culturing a host transformed with the nucleic acid molecule of claim 29. The

disclosure identifies the amino acid sequence of SEQ ID NO:2 and numerous nucleic acid sequences that encode SEQ ID NO:2. For example, the specification discloses the nucleotide sequence of SEQ ID NO:1 and polymorphic versions of SEQ ID NO:1, including those with silent C to T substitutions at positions 708, 801,1317, and 1698 (Fig. 2A, pg. 25, first full paragraph). Therefore, the nucleic acid molecule of claim 1 is fully supported by the disclosure as filed.

Regarding claim 30, the Office Action alleges that Applicants are not in possession of a nucleic acid molecule having a function as a transcription factor because allegedly there is insufficient teaching, guidance and/or working examples. Applicants respectfully assert that the specification provides evidence to support the conclusion that nucleic acid molecules of the present invention can function as transcription factors. For example, the disclosure teaches that nucleic acid molecules of the present invention encode polypeptides having Cys4-His-Cys3 double-paired finger motifs, which are known to be found in nuclear proteins that influence transcription (page 5, first paragraph). Furthermore, the disclosure as filed reveals the nuclear localization of the APGD1 protein (Example 11) and recognizes the function of the protein as a transcription factor (See claim 2 as filed). Finally, the function of the encoded APGD1 protein in the mediation or regulation of transcription is further substantiated by literature published after the filing date of the present application (See e.g., Pitkanen et al., *J. Biol. Chem.*, 276, 19597 (2001) (teaching that AIRE (the protein product of the APECED gene) activates the IFNB minimal promoter)).

Pending claims 32 to 34, 42, and 43 are directed to nucleic acid molecules that encode SEQ ID NO:6, the mouse homolog of the human APECED-associated gene. The amino acid sequence of SEQ ID NO:9, and a nucleic acid, SEQ ID NO:6, that encodes this polypeptide are disclosed in the specification as filed. Therefore, Applicants respectfully assert that a skilled artisan will recognize that the Applicants had possession of the claimed invention at the time the application was filed.

Regarding claims 36-38 and 66 which are directed at insertions, deletions, substitutions, or inversions, the Office Action alleges that the specification does not provide guidance and/or

working examples as to how to make, characterize and use loss-of-function mutants, and that there is no indication in Table 1 that the mutations cosegregate with APECED. The specification discloses that the mutants of Table 1 are mutants found in nature that cosegregate with APECED in the respective afflicted families (Page 26, last 4 sentences). Therefore, it will be recognized that the isolated nucleic acids are useful, for example, for identifying these insertions, deletions, and substitutions, thereby identifying patients carrying mutations that are linked to APECED.

Claim 41 is directed to nucleic acid molecules that contain between 27 contiguous nucleotides and full length SEQ ID NOS:1 and 6. The disclosure in providing SEQ ID NOS:1 and 6, provides the sequence of the nucleic acid molecules falling within this claim. Claim 62 is directed at a nucleic acid molecule that has the nucleotide sequence of SEQ ID NO:1, which is disclosed in the specification. Accordingly, it will be recognized that the Applicants were in possession of the invention of claims 41 and 62.

In summary, Applicants respectfully assert that the specification meets the written description requirement of 35 U.S.C. § 112, first Paragraph with respect to claims 29-38, 41-43, 48, and 62-67. Therefore, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Claim Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 30-31, 35-38, 41-43, 45-48, and 66-67 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter that applicant regards as the invention. Applicants respectfully traverse the rejection. To expedite issuance of the present application and without prejudice or disclaimer, Applicants have canceled claims 31, 35, and 67, thereby rendering moot, rejections related to these claims.

Regarding claim 30, the Office Action alleges that transcription mediator and transcription regulator are distinct compositions involving mechanistically distinct processes. Claim 30 as amended, clarifies that the polypeptide encoded by the isolated nucleic acid

molecule influences transcription of a gene (Page 6, second full paragraph). Regarding claim 36-38, the Office Action asserts that the terms "normally" and "duplication of 4 nucleotides...at position 1086-1089" renders the claim ambiguous. Claims 36-38 as amended do not include the term "normally" and clarify that the insertion can be at position 1086.

Regarding claim 41, the Office Action asserts that the claim is indefinite because of recitation of "at least about 14 nucleotides." The term "about" has been deleted from claim 41. No specific rejection was presented for claims 42, 43, or 66. Therefore, Applicants respectfully request clarification as to whether there is a specific indefiniteness rejection of these claims. Regarding claim 48, the Office Action alleges that the claim is indefinite because claim 29, from which claim 48 depends, is directed to a polynucleotide not a polypeptide. Claim 48 as amended, clarifies that the polypeptide produced is encoded by the nucleic acid molecule of claim 29. In summary, Applicants respectfully assert that claims 30-31, 35-38, 41-43, 45-48, and 66-67 are definite. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claim Rejection Under 35 U.S.C. § 102

Claims 31-32, 35, 41-44, 62, 65, and 67 stand rejected under 35 U.S.C. § 102 as being anticipated by Aaltonen et al. *Genome Res.* 820-29 (1997). To anticipate an invention, every element of a claim must be found in a single prior art reference. MPEP § 2131; Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628,631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

To expedite issuance of the present application and without prejudice or disclaimer, Applicants have canceled claims 31, 35, 44, 62, 65, and 67, thereby rendering moot, rejections related to these claims. Regarding claim 32, the Office Action asserts that Aaltonen et al. teach an isolated 350 kb polynucleotide segment from human chromosome 21q22.3 associated with APECED. The Office Action alleges that this sequence is a mammalian homolog of SEQ ID NO:1. Claim 32 as amended is directed to a polypeptide encoding SEQ ID NO:9, a mouse homologue of the human AIRE protein, which is encoded by the APECED gene. Aaltonen

provides no mouse sequence information and no other sequences that encode SEQ ID NO:9. Accordingly, Aaltonen et al. does not anticipate claim 32.

Regarding claims 41-43, the Office Action alleges that Aaltonen et al. anticipates claims 41-43 because the Aaltonen et al. polynucleotide molecules are longer than 21 contiguous nucleotides and capable of hybridizing with SEQ ID NO:1. Claim 41 is directed to a nucleic acid molecule that "consists of" between 21 and 2245 contiguous nucleotides of SEQ ID NO:1. Since Aaltonen et al. does not disclose an isolated nucleic acid molecule having a sequence of SEQ ID NO:1, it cannot anticipate claim 41. Regarding claims 42-43, these claims are directed to complements (claim 42) or DNA or RNA (claim 43) of the nucleic acid molecule of claims 29 or 35. Claim 29 recites an isolated nucleic acid molecule that includes a contiguous coding region that encodes a polypeptide according to SEQ ID NO:2. The coding region of the APECED gene is separated in the genome by introns (See e.g. Figure 1B; and Exhibit A (Genbank entry AB006684), which lists the nucleotides of the APECED gene that are joined to form the coding sequences (listed to the rights of "CDS")). Aaltonen et al. disclose large genomic clones that, even if they encompass the APECED gene, do not contain a contiguous coding sequence of SEQ ID NO:2, due to the presence of introns in the coding sequence. Furthermore, cDNAs that were reported by Aaltonen et al. as being localized to an 800 kb chromosomal region that includes the APECED gene, are not large enough to include nucleotides encoding the entire polypeptide of SEQ ID NO:2. The coding region of SEQ ID NO:1 is 1638 nucleotides (nucleotides 121-1758), wherein cDNA f9 identified by Aaltonen et al., is only 1000 nucleotides (Aaltonen et al. 825, left column first paragraph) and IMAGE clone 126541 identified by Aaltonen et al., is only 1068 nucleotides (See Exhibits B and C, dbEST listing for IMAGE clone 126541, 5' and 3' respectively).

Claims 31-32, 35, 41-43, 62, 65, and 67 stand rejected under 35 U.S.C. § 102 as being anticipated by Bjorses et al. *Am. J. Genet.* 59, 879-86 (1996). To expedite issuance of the present application and without prejudice or disclaimer, Applicants have canceled claims 31, 35, 44, 62, 65, and 67, thereby rendering moot, rejections related to these claims. Regarding

claim 32, the Office Action asserts that Bjorses et al. teach an isolated polynucleotide segment from human chromosome 21q22.3 associated with APECED. The Office Action alleges that since DNA molecules taught by Bjorses et al. are obtained from the same chromosome locus as SEQ ID NO:1, some of the DNA molecules taught by Bjorses et al., must "comprise" SEQ ID NO:1.

Claim 32 as amended is directed to a polypeptide encoding SEQ ID NO:9, a mouse homologue of the human AIRE protein, which is encoded by the APECED gene. Bjorses et al. provides no mouse sequence information and no other sequences that encode SEQ ID NO:9. Accordingly, Bjorses et al. does not anticipate claim 32.

Regarding claims 41-43, the Office Action alleges that Bjorses et al. anticipates claims 41-43 because the Aaltonen et al. polynucleotide molecules are longer than 21 contiguous nucleotides and capable of hybridizing with SEQ ID NO:1. Claim 41 is directed to a nucleic acid molecule that "consists of" between 21 and 2245 contiguous nucleotides of SEQ ID NO:1. Since Bjorses et al. does not disclose an isolated nucleic acid molecule having a sequence of SEQ ID NO:1, it cannot anticipate claim 41. Regarding claims 42-43, these claims are directed to complements (claim 42) as well as DNA or RNA (claim 43) of the nucleic acid molecule of claim 29. Claim 29 recites an isolated nucleic acid molecule that includes a contiguous coding region that encodes a polypeptide according to SEQ ID NO:2. The coding region of the APECED gene is separated in the genome by introns (See e.g. Figure 1B; and Exhibit A (Genbank entry AB006684), which lists the nucleotides of the APECED gene that are joined to form the coding sequences (listed to the rights of "CDS")). Bjorses et al. disclose large genomic clones that, even if they encompass the APECED gene, do not contain a contiguous coding sequence of SEQ ID NO:2, due to the presence of introns in the coding sequence.

Claims 32 and 65 stand rejected under 35 U.S.C. § 102 as being anticipated by Korenberg et al. U.S. Pat. No. 6,166,180. To expedite issuance of the present application and without prejudice or disclaimer, Applicants have canceled claim 65, thereby rendering moot, the rejection related to this claim. Regarding claim 32, the Office Action asserts that

Korenberg et al. teach an APECED associated polynucleotide that is isolated from human chromosome 21 in a BAC containing contig that contains the APECED gene. Claim 32 as amended is directed to a polypeptide encoding SEQ ID NO:9, a mouse homologue of the human AIRE protein, which is encoded by the APECED gene. Korenberg et al. provides no mouse sequence information and no other sequences that encode SEQ ID NO:9. Accordingly, Korenberg et al. does not anticipate claim 32.

Claims 32, 35, 41-43, and 45-47 stand rejected under 35 U.S.C. § 102 as being anticipated by Klinger et al. (U.S. Pat. No. 6,071,717). Regarding the rejected claims, the Office Action alleges that Klinger et al. teach a human polynucleotide that is greater than 21 nucleotides in length and that hybridizes to the polynucleotides of SEQ ID NO:1. None of the rejected claims as amended, recite hybridization language. All of the claims recite, or depend from a claim that recites, a nucleic acid molecule whose sequence is disclosed in the present specification, or a contiguous nucleic acid molecule which encodes a polypeptide of SEQ ID NOS:1 or 9. None of the nucleic acid molecules are disclosed in Klinger et al. Accordingly, Klinger et al. does not anticipate the invention of the pending claims.

In summary, Aaltonen et al., Bjorses et al., Korenberg et al., and Klinger et al. do not anticipate the present invention because they do not disclose nucleic acid molecules that fall within the pending claims. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102 of claims 31-32, 35, 41-44, 62, 65, and 67 over Aaltonen et al.; claims 31-32, 35, 41-43, 62, 65, and 67 over Bjorses et al.; claims 32 and 65 over Korenberg et al. and claims 32, 35, 41-43, and 45-47 over Klinger et al.

Claim Rejection Under 35 U.S.C. § 103(a)

Claims 29, 32, 34, 35, 41-48, 62, 65, and 67 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious in view of Aaltonen, J. et al. (*Genome Res.*, 7:820-829 (August 1997)) taken with Bjorses, P. et al. (*Am. J. Hum. Genet.* 59:879-86 (1996)) and Korenberg, J. R., et al. (U.S. Pat. No. 6,166,180). Applicants respectfully traverse the rejection.

To establish a *prima facie* case of obviousness there must be some suggestion or motivation in the prior art to make the claimed invention, there must be a reasonable expectation of success, and the prior art reference must teach or suggest all of the claim limitations. MPEP § 2142; In re Vaeck, 947 F.2d 488, 20 USPQ2d, 1438 (Fed. Cir. 1991). In order to be relied upon in an obvious rejection, cited art must be prior art under 35 U.S.C. § 102. MPEP § 2141.01. "In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure.'" MPEP 2121.01 citing In re Hoeksema, 399 F.2d 269, 158 USPA 596 (CCPA 1968). "'Such possession [of an enabling disclosure] is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention.'" MPEP 2121.01 citing In re Donohue, 766 F.2d 531, 226 USPQ 619 (Fed. Cir.1985). Accordingly, cited references must provide an enabling disclosure of teachings for which they are cited in an obviousness rejection.

The Office Action alleges that Aaltonen et al. teach localization of an APECED gene in a 800 kb region of human chromosome 21q22.3 using fiber fluorescent *in situ* hybridization (FISH) and primers for this gene. Furthermore, the Office Action alleges that Bjorses et al. teach localization of an APECED gene in human chromosome 21q22.3 using linkage and haplotype analysis, and suggest use of positional cloning to isolate the gene responsible for APECED. The Office Action alleges that the combination of Bjorses et al.'s suggestion to use positional cloning with Aaltonen et al.'s use of positional cloning and FISH, would lead to the invention of the rejected claims. Furthermore, the Office Action alleges that Korenberg et al. teach a gene marker located on 21q22.3 as well as vectors, hosts, and methods for producing proteins encoded by a polynucleotide.

To expedite issuance of the present application and without prejudice or disclaimer, Applicants have canceled claims 35, 44, 65, and 67, thereby rendering moot, rejections related to these claims. Applicants respectfully assert that the cited references, individually or in combination, do need teach or suggest a nucleic acid molecule according to the present claims.

Aaltonen et al., Bjorses et al., and Korenberg et al. at most, provide a series of large genomic clones at least one of which includes the APECED gene. However, none of these references teach or suggest a nucleic acid according to the pending claims because even if one of the clones disclosed in the cited references contained the APECED gene, they do not contain a contiguous coding sequence of a human or mouse APECED gene product because of the presence of introns in the coding region of the gene (See Exhibit A).

Regarding claim 41, which is directed at nucleic acid molecules that "consist of" between 21 and 2245 contiguous nucleotides of SEQ ID NO:1, or between 21 and 1656 nucleotides of SEQ ID NO:6, the clones of the cited references are too large to "consist of" these sequences, except for the cDNAs reported in Aaltonen et al. However, these cDNA clones are unrelated or not enabled by Aaltonen et al. One clone, IMAGE clone 126541, apparently is not related to the APECED coding region (See BLAST results of Exhibits E and F). Regarding the cDNA f9, identified by Aaltonen et al., no structural information is provided in Aaltonen et al. regarding this cDNA other than its size. Furthermore, the EST that is disclosed by Aaltonen et al. as being homologous to F9, 21ES212, is not present in Genbank, (See search results of Exhibit G). Accordingly, clone f9 is not enabled by Aaltonen et al. because no sequence information or other structural information is provided regarding f9, except for its 1.0 kb size. The general disclosure that the cDNA clone f9 without any structural information cannot render the presently claimed invention obvious. Accordingly, the cited prior art does not teach or suggest all the claimed limitations.

Case law supports the conclusion that the cited art cannot render the claimed nucleic acid molecules, host, or vectors obvious, if the art does not disclose the structure of the claimed nucleic acid molecules. In response to Applicants arguments in the previous Amendment, filed September 16, 2003, that the references alone or in combination do not disclose the chemical structure (i.e., nucleotide sequence) of a polynucleotide of claim 29 or claim 35, and therefore do not render the claims obvious, the Office Action alleges that Aaltonen et al.'s teachings meet the limitations of claim 29 because Aaltonen et al. allegedly teach an isolated polynucleotide

located on human chromosome 21q22.3 associated with the APECED disease state, and a bacterial clonal contig covering the important region for cloning the APECED gene.

The Office Action's allegations regarding obviousness in view of the teachings of the cited prior art, which are silent with respect to the structure of the claimed polynucleotides, are inconsistent with the Federal Circuit's line of cases clarifying obviousness requirement for biotechnology inventions. In In re Deuel (34 USPQ2d, 1210 (Fed. Cir. 1995)), affirming its prior decision of In re Bell (26 USPQ2d, 1529 (Fed. Cir. 1993)), the Federal Circuit held that claims directed at nucleic acid molecules that encode human heparin-binding growth factors (HPGFs) were not rendered obvious by prior art teaching of the isolation of human HBGFs and the disclosure of a portion of their amino acid sequence, combined with known methods of using protein sequences to synthesize primers for cloning nucleic acid molecules encoding the protein. In re Deuel, at 1215. The Federal Circuit in In re Deuel indicated that since the claims at issue claimed new chemical entities in structural terms (i.e., a nucleotide sequence of a nucleic acid molecule), "a *prima facie* case of unpatentability requires that the teachings of the prior art suggest *the claimed compounds*" (emphasis in original). Id., at 1214. The court further concluded that while the general idea of the claimed molecules, their function, and their general chemical nature may have been obvious from the cited prior art's teachings, and the knowledge that some gene existed may have been clear, the precise cDNA molecules of the claims would not have been obvious without disclosure of their nucleotide sequence. Id., at 1215.

The inventions of the pending claims are directed to isolated nucleic acid molecules that include contiguous coding regions that encode polypeptides with amino acid sequences (i.e., SEQ ID NO:2 and SEQ ID NO:9) that are disclosed in the pending application, as well as vectors, host cells and methods that include the nucleic acid molecules. As established by the Federal circuit, even if the general idea of the claimed molecules, their function, and their general chemical nature were obvious from prior art teachings, and the knowledge that an APECED gene existed may have been clear, the nucleic acid molecules of the pending claims are not rendered obvious by the cited prior art, because the cited prior art does not teach the

chemical structure (i.e. the nucleotide sequence) of the claimed nucleic acid molecules. In the present situation the prior art references at best provide tools that could be helpful in cloning the APECED gene (Aaltonen et al. page 826, right column first paragraph), but provide no information regarding the chemical structure of the gene. Therefore, according to Federal Circuit precedent, the cited references do not render the present invention obvious.

In addition to not teaching all of the claimed limitations, based on the cited references a skilled artisan would not conclude that there was a reasonable expectation of success of identifying and isolating a nucleic acid molecule that encodes the APECED gene product. The clones disclosed in Aaltonen et al., Bjorses et al., and Korenberg et al. provide no more than a series of very large clones in a region within which, as acknowledged in the cited references, it is difficult to identify coding regions, especially an APECED coding region. Aaltonen et al. provide a series of large cosmid, P1-derived artificial chromosomes (PAC), and bacterial artificial chromosomes (BAC), within a 350 kb genomic region that was believed to harbor the APECED gene based on linkage analysis. Bjorses et al. identify a 2.6 cM interval on chromosome 21q22.3 that appeared by linkage analysis to include the APECED gene. Korenberg et al. disclose a series of BACs that map to 21q22.3.

As acknowledged in the references cited in the Office Action, it was recognized that cloning the APECED gene was a particularly difficult task. Aaltonen et al., discusses the difficulties in cloning the APECED gene indicating that "[t]he chromosomal regions near centromeres and telomeres of most human chromosomes are known to be problematic for cloning and characterization because of their high content of repetitive and GC-rich sequences (Gardiner 1996). The subtelomeric region of 21q22.3 containing the APECED locus belongs to these chromosomal regions." (Aaltonen et al., page 826, left column, second full paragraph). Thus, a skilled artisan would not conclude that there was a reasonable expectation of success in identifying sequences encoding the APECED gene product based on the references cited in the Office Action. Furthermore, the cited passage from Aaltonen et al. confirms that there was a long-felt need and others failed at isolating nucleic acid molecules that encode the APECED gene product. Objective evidence of secondary considerations such as long-felt need and

failure of others are relevant to the issue of obviousness and must be considered in every case in which they are present. MPEP 2141; Stratoflex, Inc. v. Aeroquip Corp., 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987).

In summary, the cited references do not teach or suggest, alone or in combination, nucleic acid molecules according to the present invention. Therefore, the cited prior art references do not teach or suggest all of the claimed limitations. Furthermore, a skilled artisan would not conclude that there is a reasonable expectation of success in isolating a nucleic acid according to the pending claims based on the cited references. Similar to the factual situation in In re Deuel, the Office Action asserts prior art that teaches methods that allegedly would assist in the identification of a nucleic acid molecule of the pending claims, but does not provide information regarding the structure of the claimed nucleic acid molecules. Accordingly, the Office Action fails to state a *prima facie* case of obviousness. Furthermore, evidence is presented of failure of others and long-felt need. Accordingly, Applicants respectfully request withdrawal of the rejection of claims 29, 32, 34, 35, 41-48, 62, 65, and 67 under 35 U.S.C. § 103(a) as allegedly being obvious in view of Aaltonen, J. et al., taken with Bjorses, P. et al. and Korenberg, J. R., et al.

In view of the above amendments and remarks, reconsideration and favorable action on all claims is respectfully requested. Should any questions remain in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved. Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Date: June 3, 2004

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